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the *lacZ* (β -galactosidase) and *hph* (hygromycin phosphotransferase) genes into the pronucleus of fertilized bovine oocytes.

As described in the DECLARATION, fluorescence *in situ* hybridization (FISH) analysis of blastocysts using probes specific for the artificial chromosome revealed that 27% of the embryos obtained after pronuclear injection scored positive for the presence of the satellite DNA-based artificial chromosome. On average, 27% of the cells of the positive embryos contained the artificial chromosomes as discrete chromosomes. The results of these analyses demonstrate that satellite DNA-based artificial chromosomes as described in the above-referenced application can be used in standard methods employed in the generation of transgenic animals to yield viable bovine embryos containing the artificial chromosomes in their cells.

A previous Declaration of Perez under 37 C.F.R. §1.132 (submitted March 31, 2000) demonstrated that using materials and methods described in the subject application and standard methods of transgenic animal production, transgenic mice containing satellite DNA-based artificial chromosomes that are transmitted through the germline could be produced. The further DECLARATION of Perez, provided herewith, demonstrates that, similarly, bovine embryos containing essentially the same satellite DNA-based artificial chromosomes can be produced. The bovine embryos containing the artificial chromosomes should be suitable for transfer into female recipient cows for development into transgenic cows. Although certain of the procedures utilized in generation of the transgenic bovine embryos are somewhat specific for production of transgenic bovine (for example, *in vitro* fertilization of the bovine oocyte), many of the basic oocyte handling and microinjection procedures were similar or identical to those used in generation of transgenic mice.

As discussed in the Preliminary Amendment submitted December 21, 2000, those of skill in the art of transgenic animal generation recognize similarities in the production of transgenic mice and other transgenic animals, particularly bovine species. Clearly, the results described in the DECLARATION of Perez submitted herewith are supportive of a correlation between mouse and other transgenic animal systems as it was possible to generate transgenic bovine embryos just as it was possible to generate transgenic mouse embryos as demonstrated in the previous

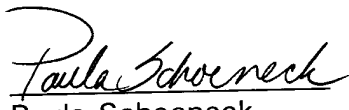
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Perez Declaration. Therefore, it is respectfully submitted that Applicant has provided ample evidence that, as set forth in the subject application, the artificial chromosomes taught therein may be used in methods of producing transgenic animals of a variety of species.

In view of the above remarks and the amendments and remarks of record, reconsideration and allowance of the application are respectfully requested.

Respectfully submitted,
HELLER EHRMAN WHITE & McAULIFFE LLP

By:


Paula Schoeneck
Registration No. 39,362

Attorney Docket No. 24601-402A
Address all correspondence to:
HELLER EHRMAN WHITE & McAULIFFE LLP
4250 Executive Square, 7th floor
La Jolla, CA 92037-9103
Telephone: 858/450-8400
EMAIL pschoeneck@hewm.com